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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/049,865	03/27/1998	COLLIN J. WEBER	47765/CJPW/	6162

7590 07/16/2003

Cooper & Dunham, LLP
1185 Avenue of the Americas
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EXAMINER

DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 07/16/2003

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/049,865

Applicant(s)

WEBER ET AL.

Examiner

MINH-TAM DAVIS

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 April 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 54-70 is/are pending in the application.
- 4a) Of the above claim(s) 60 and 61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 54-59, 62-70 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The finality of the previous Office action has been withdrawn, and the prosecution of this application is reopened .

It is noted that applicant has paid for a Notice of Appeal. Applicant can either request a refund or place the funds on credit for future appeals.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 1, 2, 4-7, 9-14, 16, 17, 20, 23 and 43-47, and adds new claims 48-64.

New claims 48-64 have been renumbered as 54-70, according to rule 126.

New claims 54, 60-61 are drawn to a method for transplanting into a subject a viable xenogeneic cell or tissue, comprising transplanting the cell or tissue into the subject, wherein the cell or tissue is surrounded by a semipermeable membrane that is impermeable to immunoglobulins, and treating the subject with a prophylactically effective amount of an agent which inhibits an immune system costimulation event mediated by a cell surface molecule selected from the group consisting of GP39, CD40 and CD4, wherein the agent is GK1.5 or MR1,

Since applicant has received an action on the merits for the originally presented invention, drawn to a method for transplanting into a subject a viable xenogeneic cell or tissue, comprising transplanting the cell or tissue into the subject, wherein the cell or tissue is surrounded by a semipermeable membrane that is impermeable to immunoglobulins, and treating the subject with a prophylactically effective amount of an agent which

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inhibits an immune system costimulation event mediated by a cell surface molecule selected from the group consisting of B7, CD28 or CTLA4, wherein the agent is CTLA4 or CTLA4Ig, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, part of claim 54, and claims 60-61 are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03.

Newly submitted claims 54, 60-61 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The originally presented product invention and the newly added method as disclosed are distinct from each other because they differ at least in method steps, reagents and/or dosages, and/or schedules used, and response variables, and are therefore distinct inventions.

Accordingly, claims 54-59, 62-70 are examined in the instant application, wherein claims 54-59, 62-70 are examined only to the extent of a method for transplanting into a subject a viable xenogeneic cell or tissue, comprising transplanting the cell or tissue into the subject, wherein the cell or tissue is surrounded by a semipermeable membrane that is impermeable to immunoglobulins, and treating the subject with a prophylactically effective amount of an agent which inhibits an immune system costimulation event mediated by a cell surface molecule selected from the group consisting of B7, CD28 or CTLA4, wherein the agent is CTLA4 or CTLA4Ig. Claims 60-61 are withdrawn from consideration as being drawn to non-elected invention.

INFORMATION DISCLOSURE STATEMENT

It is noted that the PTO-1449 and the references of the information disclosure statement of paper No:15, on 03/04/02 are missing. Applicant is invited to submit the PTO-1449 and the references for consideration.

OBJECTION

Claim 54 is objected to because part of claim 48 is drawn to non-elected invention, i.e. a method for transplanting into a subject a viable xenogeneic cell or tissue, comprising transplanting the cell or tissue into the subject, wherein the cell or tissue is surrounded by a semipermeable membrane that is impermeable to immunoglobulins, and treating the subject with a prophylactically effective amount of an agent which inhibits an immune system costimulation event mediated by a cell surface molecule selected from the group consisting of GP39, CD40 and CD4.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Claims 54-57, 62-70 are rejected under 35 USC 112, first paragraph, pertaining to lack of enablement for "any agent" which inhibits an immune system costimulation event, for reasons already of record in paper No.11 .

Applicant argues that new claims 48-53, 56-63 now provide a method wherein the agent administered inhibits a costimulation event mediated by one of several cell surface molecules including B7, CD28, CTLA4, GP39, CD40 and CD4, thus limited to defined costimulation events.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

Rejection remains because the specification discloses that a "substance" which inhibits an immune system costimulation event, includes, "but not limited to", T cell or APC cell surface-molecule "analogs" (p.27). In other words, due to the language "but not limited to", and T cell or APC cell surface-molecule "analogs", a substance or an agent which inhibits an immune system costimulation event could be any compound, including T cell or APC cell surface molecules which have been modified, deleted, truncated, substituted, conjugated etc.. Applicant has not enabled for the claimed inhibitory agent, regardless whether the costimulation events are limited to those mediated by one of several cell surface molecules including B7, CD28, CTLA4, GP39, CD40 and CD4.

REJECTION UNDER 35 USC 103

Claims 54-59, 62-70 are rejected under 35 USC 103, pertaining to obviousness over Lenschow et al, in view of Goosen et al, Soon-Shiong et al, Akalin et al, Linsley et al, Padrid et al, and Steurer et al for reasons already of record in paper No.11.

New claims 54-59, 62-7 are drawn to a method for transplanting into a subject a viable xenogeneic cell or tissue, comprising transplanting the cell or tissue into the subject, wherein the cell or tissue is surrounded by a semipermeable membrane that is impermeable to immunoglobulins, and treating the subject with a prophylactically effective amount of an agent which inhibits an immune system costimulation event

mediated by a cell surface molecule selected from the group consisting of B7, CD28 or CTLA4, wherein the agent is CTLA4 or CTLA4Ig, and wherein the semipermeable membrane comprises polylysine-alginate, or is a microcapsule or is double-walled.

Applicant argues that the results are unexpected. The graft survival with both CTLA4Ig and microencapsulation together is over 4- fold longer than with microencapsulation alone and over 20-fold longer than with CTLA4Ig alone. Nothing in the cited references would permit one to foresee such a dramatic increase.

Applicant's arguments set forth in paper No.12 have been considered but are not deemed to be persuasive for the following reasons:

One of ordinary skill in the art would have expected that the combination of CTLA4Ig and microencapsulation together would increase the chance of preventing graft rejection, better than with microencapsulation alone or with CTLA4Ig alone, because CTLA4Ig and microencapsulation complement each other. That is CTLA4Ig inhibits T cell activation, cell-mediated and humoral immune response, prevents macrophage activation and infiltration into the graft site, and inhibits immunoglobulin secretion, as taught by Lenschow et al, Akalin et al, and Linsley et al, whereas microencapsulation is impermeable to immune system proteins, and protects the transplanted cells from both cytotoxic T-lymphocytes and natural killer cells, as taught by Goosen et al and Soon-Shiong et al.

Moreover, MPEP 2145 teaches that a mere recognition of additional advantages which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. *Ex parte*

Obiaya, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). MPEP 2145 further teaches that a mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art.

Concerning newly added property of the semipermeable membrane in claims 49, 52, i.e. the semipermeable membrane comprises polylysine-alginate, or is double-walled, the semipermeable membrane used in the claimed method is obvious, because microcapsules made of polylysine and alginate for use with transplanted pancreatic cells is taught by Soon-Shiong et al (p.216, first column, paragraph under Microcapsulation procedure), and because double-walled microcapsule is well known in the art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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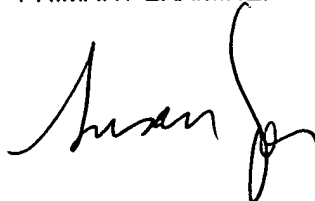
extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Susan Ungar', with a stylized flourish at the end.

MINH TAM DAVIS